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REMARKS

Claims 1, 2, 14-20 and 26-32 are pending in the application. Claims 3-13, 21-25 and 33-38 have been withdrawn.

Claim rejections - 35 U.S.C. § 112

Claims 1, 2, 14-20 and 26-32 have been rejected under 35 U.S.C. § 112, first paragraph. The Examiner has maintained her rejection of the claims as containing subject matter which was not described in the specification. The Examiner further stated that the declaration submitted on June 8, 2006 is insufficient to overcome this rejection. The declaration presented an SIV model in non-human primates and a FLV disease mice model, which is allegedly nonanalogous to the claimed method of prophylaxis and treatment of HIV in humans. The Examiner further cited Jefferys *et al.* to support the argumentation that SIV is known in the art not to be predictive of the HIV in humans because the monkey body react differently to the HIV vaccine than the human body. Thus, the instant claims are not enabled for the method for the prophylaxis or treatment of an HIV infection in a human. In order to overcome this rejection, Applicants respectfully point out that, contrary to the Examiner's position, several scientific publications demonstrate that the animal model consisting of a macaque infected with SIV and SIV-derived (chimeric) viruses demonstrates the activity of antiviral drugs that are known to be active in humans and FDA approved (i.e. PMEA, PMPA, efavirenz, AZT, 3TC and lopinavir/ritonavir). For example, Silvera *et al.* (2000) showed that PMEA (adefovir) and PMPA (tenofovir) in monotherapy could modulate the kinetics of viral loads in responsive animals, and concluded that the degree of virus dissemination was predictive of the outcome of the drug treatment. In another example, Van Rompay *et al.* (2001) demonstrated a protection against SIV transmission in macaques using prophylactic treatments with PMPA. Hofman *et al.* (2004) also demonstrated a reduction of viral titer in macaques infected with a chimeric SIV (bearing the HIV reverse transcriptase (RT) to make it susceptible to the RT inhibitor tested) using efavirenz. Yoshimura *et al.* (2003) tested a highly active antiretroviral therapy (HAART) in macaques infected with a chimeric SIV using a combination of AZT, 3TC and Lopinavir/Ritonavir and showed a reduction in viral titer. Also, North *et al.* (2005) showed that HAART with efavirenz, 3TC and PMPA was able to potently reduce the viral titer in macaques infected with a chimeric SIV. These authors concluded that the

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results mimicked HAART of HIV-infected humans. All these references, which are enclosed herewith for Examiner's convenience, not only demonstrate that studies in monkeys are predictive of the outcome of the drug treatment in humans, but also that the SIV model is a predictive model in order to evaluate the effectiveness of commercialized drugs for treatment or for the prophylaxis of an HIV infection in a human.

In addition, the Examiner alleges that "SIV is known in the art not to be predictive of the HIV in humans because the monkey body may react differently to an HIV vaccine than the human body" and gives the example of a Merck vaccine candidate (Jefferys, 2005). Applicants submit that this example is irrelevant to the subject matter claimed in the present application. The antiviral oligonucleotides taught in the present application are antiviral compounds or drugs that inhibit viral growth or replication. A person skilled in the art would acknowledge that a vaccine comprises an antigen or antigens (or a DNA coding for an antigen) stimulating the immune system which will target such antigen(s) displayed on a microorganism, (or on a cell, or as a molecule e.g. a toxine) in order to destroy the microorganism or inhibit its growth cycle. A vaccine requires the immune system of an organism to be active. The present application teaches antiviral compounds that do not comprise an antigen stimulating the immune system. In the case of antiviral compounds or drugs, replication cycle of the virus is targeted by the compound itself and not through stimulation of the immune system. Moreover, the Examiner referred to the Merck vaccine candidate (Jefferys, 2005) to allege that the SIV infected macaque model is not predictive. To the contrary, Applicants point out that this reference teaches the opposite. Indeed, the vaccine platform, naked DNA and adenovirus (Ad5) showed activity in humans. The naked DNA vaccine was marginally immunogenic in humans but it was still immunogenic, and the marginal response could be due to lack of optimization of the vaccine. The Ad5 vaccine induced a good immunologic response in a subgroup of humans, proving that the macaque model can be predictive. The Ad5 vaccine was only active in a subgroup of humans and not active in another subgroup because of pre-immunisation against the adenovirus (viral carrier) portion itself in the second group. Furthermore, Applicants respectfully point out that the vaccine referred in Jefferys was not tested for its protective effect, which is the concluding test to be done when measuring the effect of a vaccine. Thus, it is believed that the Examiner has presented an example of a vaccine that was tested in the monkey body and which was marginally immunogenic in humans.

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Consequently, the Examiner's own example demonstrates that the macaque model can be predictive.

The Examiner also stated that "the art of HIV gene therapy is highly unpredictable". Applicants respectfully submit that, contrary to the argument presented by the Examiner, the antiviral oligonucleotides taught in the present application are antiviral compounds or drugs that directly inhibit the viral growth or replication, and cannot be considered as a gene therapy or related to a gene therapy. In fact, gene therapy is defined by the delivery of a DNA coding for a protein(s) having a desired effect and is unrelated to the subject matter claimed in the present application. The oligonucleotides of the present invention do not code for a protein. Thus, Applicants believe that the Examiner's argument that the present application is directed to a gene therapy in order to ascertain its unpredictability is not relevant to the present invention.

Finally, Applicants respectfully submit that it is stated in the Manual of Patent Examining Procedure that:

> "If reasonably correlated to the particular therapeutic or pharmacological utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will ***be sufficient to establish therapeutic or pharmacological utility*** for a compound, composition or process.
>
> Office personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials. There is no decisional law that requires an applicant to provide data from human clinical trials to establish utility for an invention related to treatment of human disorders."

In view of the efficacy of the method claimed in the present application to treat *in vivo* models following viral infection, and in view of the teaching found in Silvera *et al.* (2000), Van Rompay *et al.* (2001), Hofman *et al.* (2004), Yoshimura *et al.* (2003) and North *et al.* (2005), all references demonstrating that studies in monkeys are predictive of the outcome of the drug treatment in humans and also that the SIV model is a predictive model in order to evaluate effectiveness of commercialized drugs or treatment for the prophylaxis or treatment of an HIV

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infection in a human, there is credibility in asserting utility for treating HIV infection in a human by means of the present invention.

In view of the foregoing, reconsideration and withdrawal of the Examiner's rejection of claims 1, 2, 14-20 and 26-32 under 35 U.S.C. § 112, first paragraph, are respectfully requested.

New Claim Objections

Claim 1 has been amended to correct the grammatical error as required by the Examiner.

New Claim Rejections – 35 USC § 112

Claims 1, 2, 14-20, and 26-32 have been rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement. The Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Examiner further stated that the newly-amended limitation "sequence independent mode of action" encompasses all possible targets related to HIV and that the specification lacks sufficient variety of species to reflect this highly variable genus. Further, the specification only provides a description of 45 oligonucleotides, of which only 26 have nucleotide sequence identity. The remaining 19 oligonucleotides in Table 1 disclose only the length of the oligonucleotide. Therefore, 26 sequences do not constitute a representative number of species to adequately describe such a broad genus of oligonucleotides. In order to overcome this rejection, Applicants respectfully submit that the 19 oligonucleotides found in Table 1, which are described by the Examiner as being identified only by the length of the oligonucleotide, represent randomer oligonucleotides. As defined on page 14 of the present description, the term "randomer" is intended to mean a single stranded DNA having a wobble (N) at every position, such as NNNNNNNNNN. Each base is synthesized as a wobble, such that the randomer oligonucleotides of the present invention actually consist of a population of different randomly generated sequences of the same size. By the nature of the preparation used to produce them, a sequence complementary mode of action cannot occur. It is believed that a person skilled in the art would recognize that the only common feature between the 26 oligonucleotides having a

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specific sequence and the 19 randomer oligonucleotides disclosed in Table 1 is that they have anti-HIV activity occurring by a sequence independent mode of action. As disclosed on page 11 of the present description, in a 15 μmol preparation of a randomer oligonucleotide containing 32 nucleotides in length, this preparation will have at most 2 copies of every possible sequence of nucleotides. Thus, the presence of 2 copies of a specific sequence cannot account for the response observed in the present application. For the disclosed 19 randomer oligonucleotides of Table 1, by the nature of the preparation used to produce them, a sequence complementary mode of action cannot occur. In addition, Applicants respectfully point out that it is stated in the Manual of Patent Examining Procedure that:

> "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the genus" (Manual of Patent Examining Procedure 2163.05)."

It is thus believed that the present description discloses 45 oligonucleotides, of which 26 have nucleotide sequence identity and 19 are randomer oligonucleotides. In addition, the present description discloses 45 oligonucleotides of differing lengths. The 19 randomer oligonucleotides, acting by a sequence independent mode of action, are by themselves a representative number of species, and of the genus itself, as they are independent of any specific sequence. Thus, it is believed that the present application teaches a sufficient and/or representative number of varieties of species to reflect the highly variable genus.

In view of the foregoing, reconsideration and withdrawal of the Examiner's rejection of claims 1, 2, 14-20 and 26-32 under 35 U.S.C. § 112, first paragraph, are respectfully requested.

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It is submitted, therefore, that the claims are in condition for allowance. Reconsideration of the Examiner's rejections is respectfully requested, and allowance of claims 1, 2, 14-20 and 26-32 at an early date is solicited.

No additional fees are believed to be necessitated by this amendment. Should this be in error, authorization is hereby given to charge Deposit Account No. 19-5113 for any underpayment or to credit any overpayment.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,

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Enc.: -Copy of Silvera *et* al. (2000), Van Rompay *et al.* (2001), Hofman *et al.* (2004), Yoshimura *et al.* (2003) and North *et al.* (2005).